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TECH CENTER 1600/2900

SEQUENCE LISTING

<110> Montminy, Marc R.

<120> Methods for Treating Diabetes Mellitus

<130> SALK1650-1

<140> US 08/961,739

<141> 1997-10-31

<150> US 194,468

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| | | Thr | 20 | _ | | | | 25 | | | | | 30 | | |
| Asp | His | Arg 35 | Phe | Phe | Asp | His | Cys 40 | Cys | Asp | Leu | Leu | Lys 45 | Pro | Pro | Pro |
| Pro | Pro 50 | Pro | Ser | Pro | Pro | Gly 55 | Glu | Leu | Leu | Pro | Phe 60 | Phe | Thr | Val | Gly |
| Gly 65 | Leu | Val | Pro | Pro | Pro 70 | Pro | Pro | Asp | Ala | Ala 75 | Ala | Gln | Thr | Asn | Cys 80 |
| - | | Leu | | 85 | _ | _ | | | 90 | | | | | 95 | |
| Ser | Thr | Gln | Gln 100 | Ile | Gly | Gly | Cys | Glu 105 | Cys | Cys | Ala | Ala | Leu 110 | Leu | Gln |
| | | Pro 115 | | | | | 120 | | | | | 125 | | | |
| Arg | Ser 130 | Thr | Asn | Asn | Gly | Gln 135 | Gln | Val | Pro | Pro | Gly 140 | Lys | Ser | Ser | Ser |
| 145 | | Pro | | | 150 | _ | _ | | | 155 | | | | | 160 |
| | | Gly | | 165 | | | | | 170 | | | | | 175 | |
| | | Ala | 180 | | | | | 185 | | | | | 190 | | |
| | | Ala 195 | | | | | 200 | | | | | 205 | | | |
| Thr | Thr 210 | Trp | Trp | Ser | Ala | Ala 215 | Asn | Phe | Phe | Phe | Phe 220 | Phe | Asn | Gln | Thr |
| Thr 225 | Pro | Arg | Pro | Pro | Ser 230 | Ile | Ile | Asn | Ser | Gly 235 | Gly | Leu | Asn | Asn | Ile 240 |

Arg Arg Arg Arg Arg Asn Lys Gly Gly Ala Gln Gln His Glu Trp Trp Leu Leu Gly Gly Ala Gly Gly Arg Lys Gly Gly Gly Gly Gly Gly Trp Asn Asn Pro Thr Leu Leu Pro Ala Met Met Gly Gly Gln Ala Val Val Leu Ala Glu Glu Glu Glu Thr Leu Thr Thr Gly Phe Pro Pro Lys Trp Trp Gly His Ala Ala Thr Lys Tyr Tyr His Arg Arg Arg Arg Arg Arg Glu Ala Lys Met Met Asn Asp Trp Trp Pro Gln Val Val Phe Gly Gly Thr Leu Asn Trp Trp Gly Ser Arg Arg Gly Ala Thr Thr Ser Glu Glu Pro Ser Ser Lys Gln Gln Gln Gln Ser Met Val Val Phe Thr Thr Leu Phe Phe Thr Asp Ile Ile Glu Tyr Phe Phe Ser Pro Pro Pro Pro Pro Cys Gln Ile Ile Ser Gln Gln Ala Asn Ile Ile Trp Glu Leu Leu Pro Thr Thr Ser Asn Cys Cys Cys Cys Cys Arq Pro Pro Gln Gln Thr Thr Glu Lys Arg Arg Thr Asp Asp Ser Ser Ser Ser Val Leu Leu Leu Leu Leu Leu His Ala Ala Gln Met Ser Ser Asp Glu Glu Gln Ala Asn Asn Arg Gly Ser Xaa Pro Val Val Val Val Val Ser His Thr Thr Arg Thr Thr Glu Lys Arg Arg Ile Thr Thr Thr His His Ser Gly Ser Ser Ser Ser Ser Ser Leu Leu Lys Leu Pro Pro Cys Ala Ser Ser Thr Thr Thr Ser Ser Leu Leu Trp Lys Asn Asn Asn Asn Cys Thr Arg Arg Leu Ser Ser Phe Ala Ala Pro Leu Lys Lys Cys Gln Ser Glu Glu Glu Glu Glu Glu Asn Lys Pro Pro Leu Gly Gly Ser Ser Glu Phe Lys Lys Thr Ile Ile Phe Cys Trp Trp Trp Trp Trp Arg Ala Ala Arg Met Pro Pro Ser Leu Ser Ser Pro Lys Lys Pro Thr Thr Ser Ser Met Met Met Met Gln Arg Ala Ala Cys Cys Ser Ser Asp Ser Ser Tyr Met Asn Asn Ala Ser Asp Asp Ser Cys Cys Cys Cys Cys Leu Arg Phe Phe Gly Gln Gln Thr Ser Thr Thr

| | 610 | | | | | 615 | | • | | | 620 | | | | |
|-----|------------|-------|-------|-----|----------|----------------|--------------|-------|------------|-------|-------------|--------|--------|------------|------|
| Leu | | Pro | Pro | Gln | Gln | | | | Ser | Ser | | Ser | Ser | Ser | Cys |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Pro | Pro | Glu | Thr | Thr | Thr | Met | Ser | Val | Val | Ser | Arg | Arg | Glu | Gln | Gln |
| | | | | 645 | | | | | 650 | | | | | 655 | |
| Asp | Gln | Gln | | Gln | Gln | Gln | Pro | | Asn | Asn | Asp | Phe | | Arg | Gln |
| | | | 660 | | | | | 665 | | | | | 670 | 1 | |
| Leu | Leu | | Thr | Ser | Ser | Gly | | | | | His | | His | His | His |
| | | 675 | | ^ | 3 | 70 | | 112 - | | | 7.1. | 685 | C | m 1 | т1. |
| His | | Met | Met | Ser | Asn | 695 | Trp | HIS | HIS | GIU | 700 | ser | ser | Thr | тте |
| т1. | 690 | C 0 T | C 0 x | 802 | Sor | | Sor | Sor | Sar | Dho | | 7.1 a | Τ.Δ11 | Val | V=1 |
| 705 | ıyı | ser | ser | ser | | ser. | | | | 715 | rne | пта | пец | Vai | 720 |
| | T.vs | Glv | Glv | Δla | | | | | | | Ara | Ara | Ara | Arg | |
| Arg | цуз | Gry | GIY | 725 | Mec | пси | пси | пор | 730 | ***** | 1119 | *****9 | **** 9 | 735 | 501 |
| His | Leu | Leu | Pro | | Thr | Phe | Lvs | Lys | | Phe | Pro | Pro | Ser | Arg | Pro |
| | | | 740 | | | | | 745 | | | | | 750 | _ | |
| Pro | Gln | Leu | Leu | Leu | Leu | Leu | Leu | Lys | Ile | Ala | Ala | Met | Glu | Glu | Pro |
| | | 755 | | | | | 760 | | | | | 765 | | | |
| Gly | Cys | Cys | Met | Leu | Arg | _ | Val | Glu | Glu | Arg | | Val | Val | Val | Val |
| | 770 | | | | | 775 | | | | | 780 | | _ 4 | | |
| | Val | Val | Cys | Cys | | | | | Glu | | | | Phe | Ile | |
| 785 | _ | _ | _ | _ | 790 | | - 1 | | - 1 | 795 | 01 . | | C1 | C1 | 800 |
| Gln | Arg | Lys | Lys | | | | IIe | ITe | 11e 810 | TTE | | гàг | Glu | Glu 815 | Arg |
| 71 | T | T | C1 | 805 | C1., | | T 011 | uic | | | | Hic | Hic | Trp | V=1 |
| Arg | гуѕ | гуѕ | 820 | сту | GTÀ | Arg | ьеu | 825 | птэ | | Ary | 1115 | 830 | тър | vaı |
| Val | Val | Val | | Val | Ser | Gln | I.e.ii | | | | Ala | Trp | | Ser | Ser |
| Val | Val | 835 | , a r | Val | 001 | 0111 | 840 | 200 | 110 | 1114 | | 845 | 0-1 | 552 | |
| Pro | Leu | | Pro | Pro | Pro | Val | | Cys | Cys | Cys | Cys | | Thr | Ser | Ser |
| | 850 | | | | | 855 | - | - | - | - | 860 | _ | | | |
| Met | Gly | Pro | Pro | Pro | Leu | Pro | Pro | Glu | Ser | Ser | Cys | Arg | -Phe | Phe | Gln |
| | | | | | | | | | | | | | | | |
| Gly | Met | Met | Met | | Met | Asn | Ser | Phe | | Pro | Asn | Val | Val | Trp | Glu |
| | | _ | | 885 | | | | | 890 | _ | _ | _ | _ | 895 | _ |
| Glu | Val | Gln | | Leu | Thr | Gly | Thr | | Trp | Asp | Asp | Asp | | Asp | Asp |
| | ~ 1 | _ | 900 | D | 14 - L | N 4 - L | D | 905 | C | C | 7 | mb | 910 | Mot | 7.1. |
| vaı | GIN | 915 | Pro | Pro | мет | мес | 920 | ьeu | Cys | Cys | Arg | 925 | TIIT | Met | Ата |
| ЛΊэ | Sor | | Glv | Glv | Glv | Glv | | Glv | Glv | His | His | | T.eu | His | His |
| Ата | 930 | Ser | Сту | Gry | Ory | 935 | OLY | Oly | Ory | 5 | 940 | БСС | БСС | | |
| Met | | Gln | Gln | Ser | Lvs | | Trp | Ala | Ala | His | | Asn | Asn | Asn | Asn |
| 945 | 0 | | | | 950 | - , - | - - F | | | 955 | | | | - | 960 |
| | Asn | Ile | Met | Met | | Gly | Thr | Thr | Leu | | Arg | Gln | Phe | Leu | Leu |
| | | | | 965 | | | | | 970 | | | | | 975 | |
| Thr | Glu | Pro | Pro | Phe | His | His | His | | His | His | Pro | Val | | Gly | Met |
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| | | | | | | | | | | | | | | | |

| Ser Ser Glu Gln Cys Cys Ala Trp Gly Gly Pro Ala Ala Pro Gly Arg 995 1000 1005 | 3 |
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| 1025 1030 1035 104 | 4 |
| Ala Leu Leu His Gln Gln Thr Gln Ser Ser Ile Ala Pro Pro Leu His 1045 1050 1055 | 3 |
| His His His His Leu Leu Pro Pro Ala Ala Ala His Ala Leu Leu 1060 1065 1070 | 1 |
| Ser Asn Ile Ile Thr Ala Ala Arg Asn Asp Asp Asp Asp Asp Ser 1075 1080 1085 | r |
| Ser Ser Gln Gln Leu Leu Thr Gln Pro Pro Tyr Ser Ser Cys His Leu 1090 1095 1100 | ג |
| Leu Gln Thr Pro Pro Pro Pro Pro Thr Pro Thr Trp Leu Ser Ser | r |
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| Pro Ala Ala Gln Thr Thr Glu Tyr Pro Pro Gln Ser Ser Ser | |
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| Pro Val Gln Gln Thr Ile Cys Cys Cys Cys Cys Cys Tyr Ser Ser Ser | r |
| 1155 1160 218 278 278 278 278 278 278 278 278 278 27 | _ |
| His His Gln Gln Pro Pro Ala Cys Cys Ile Leu Ser Ser Pro Gly | y |
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| Thr Thr Thr Thr Pro Leu Ser Ser Gly Ser Ser Ser Ala Leu Leu | ı |
| 1185 1190 1195 120 | |
| Asn Arg Val Val Tyr Ser Leu Leu Leu Val Leu Lys Lys Ser Ser Ser | r |
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| Ala Ala Arg Arg Pro Met Cys Cys Met Leu Leu Asn Glu Asp Asp Asp | o |
| 1220 1225 1230 | |
| Asp Asp Asp Gly Ala Ala Gln Met Met Glu Pro Glu Glu Tyr Pro | 2 |
| 1235 1240 1245 | |
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| 1250 1255 1260 | • |
| Phe Phe Lys Val Val Ser Gln Val Val Arg Arg Asp Asp Ile Arg Arg | a |
| 1265 1270 1275 128 | |
| Arg Arg Arg Ser Arg Ser Ser Glu Pro Pro Gly Ser Arg Arg Lys | |
| 1285 1290 1295 | _ |
| | v |
| Ard Ash Ash Gill val val Ser Giv Ser Ser Ser Ser Ser Ser Ser Ard Giv | |
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| 1300 1305 1310 | |
| 1300 1305 1310 Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His | |
| 1300 1305 1310 Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His 1315 1320 1325 | s |
| Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His 1315 Pro Ser Gln Gln Gln Gln Gln Pro Arg Lys Lys Asn Leu Pro Arg Arg | s |
| 1300 1305 1310 Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His 1315 1320 1325 Pro Ser Gln Gln Gln Gln Gln Pro Arg Lys Lys Asn Leu Pro Arg Arg 1330 1335 1340 | s |
| 1300 1305 1310 Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His 1315 1320 1325 Pro Ser Gln Gln Gln Gln Gln Pro Arg Lys Lys Asn Leu Pro Arg Arg 1330 1335 1340 Leu Arg Gln Gln Thr Tyr Ala Ala Leu His Ser Ile Ile Gln Asp Asp | s g |
| 1300 1305 1310 Gly Lys Arg Thr Thr Ser Asn Asp Asp Ser Leu Leu Asn Gln His His 1315 1320 1325 Pro Ser Gln Gln Gln Gln Gln Pro Arg Lys Lys Asn Leu Pro Arg Arg 1330 1335 1340 | s g p |

| 1 | .365 | 1370 | 1375 |
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| His Arg Ala Ala I 1410 | Tle Lys Lys Pro Trp 1415 | Gln Gln Cys Gly 1420 | Ser Gly Gly |
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| 1730 | 1735 | 1740 | |

Cys Pro Pro Thr Lys Tyr Tyr Gly Cys Val Val His Ile Ile Trp Thr Thr Ile His Phe Phe Phe Phe Phe Arg Pro Pro Leu Pro Pro Pro Gln Leu Leu Tyr His Glu Glu Pro His Arg Arg Ile Ser Ser Ser Ser Ser Met Arg Arg Leu Val Val Cys Asp Ser Ser Ile Phe Gly Gly Cys Pro Pro Lys Arg Arg Arg Arg Arg Leu Leu Ser Phe Ile Ile His Pro Pro Pro Glu Glu Ser Pro Asn Asn Lys Arg Leu Leu Leu Leu Gln Glu Trp Trp Gln Glu Asp Asp Trp Thr Thr Ala Phe Ala Ala Glu Asp His His Thr Thr Thr Thr Thr Thr Arg Thr Ser Ser Lys Gln Gln Glu Arg Arg Gly Ser Arg Arg Ala Lys Lys Val Ala Leu Leu Leu Leu Leu Arg Arg Ile Ser Gly Gly Asn Val Leu Leu Arg Lys Lys Leu Arg Asn Asn Glu Lys Arg Arg Val Val Ala Ala Ser Ser Asp Ser Ala Val Val Val Val Val Val Thr Ala Ala Asn Ala Ala Glu Lys Glu Glu Thr Arg Arg Arg Asn Lys Lys Gln Lys Gln Gln Gln Gln Gln Pro Pro Pro Thr Arg Arg Lys Pro Ser Ser Ala Gln Gln Phe Pro Thr Thr Leu Ser Gln Gln Gln Gln Lys Leu Tyr Tyr His His Gly Gly Ser Thr Thr Glu Val Phe Phe Cys Asp Ser Ser Cys Met Met Met Met Met Gly Leu Leu Ser Thr Thr Ala Pro His His Trp Thr Leu Leu Pro Leu Leu His Gly Gly Glu Met Met Phe Leu Thr Thr Gly Gln Gln Thr Ser Thr Thr Glu Phe Ser Ser Ser Ser Ser Leu Arg Arg Leu Gln Met Met Pro Leu Leu Cys Met Leu Leu Gly Ala Ala Ala His Arg Arg Arg Arg Arg Arg Thr Ala Ala Val Tyr Tyr Leu Gln Ala Asn Thr Thr Val Glu Glu Thr Leu Ala Ala Ala Ala Ala His Cys Cys Val Arg Thr Thr Asp Leu Cys Cys Gln Leu Leu Thr

| | | | 2115 | 5 | | | | 2120 |) | | | | 2125 | 5 | | |
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| | Thr | Gln | | | His | Thr | Thr | Thr | Thr | Thr | His | Lvs | Met | Met | Glu | Val |
| | | 2130 | | | | | 2135 | | | | | | | | | |
| | Glv | | | Δla | Asn | Asp | | | | | | | | Ser | Ser | Ser |
| | 2145 | _ | AΙα | ALG | пор | 2150 | | Olu | 01 | 01 | 2155 | | | | | 216 |
| | | | C 0 x | C0.5 | Dro | | | Dro | Gln | Gln | | | Δla | Δla | Ser | |
| | Ser | ser | ser | ser | | | AI,g | PIO | GIII | |) | | Ата | лта | 2175 | |
| | _ | _ | <u>.</u> . | | 2165 | | | ъ. | D | | | | D | 7.1. | | |
| | Ser | Seŗ | Arg | | | Pro | vaı | Pro | | | Pro | Pro | Pro | | Cys | Cys |
| | | | | 2180 | | _ | | • | 2185 | | | _ | _ | 2190 | | _ |
| | Ala | Sęr | | | Asn | Ala | Asn | | | Thr | Thr | Arg | | | Ala | Lys |
| , | • | | 2195 | | | | | 2200 | | | | | 2205 | | | |
| | Met | Lys | Lys | Lys | Lys | Lys | | | Val | Val | Ala | | | Gln | Ala | Ala |
| | | 2210 | | | | | 2215 | | | | | 2220 | | | | |
| | Ala | Arg | Lys | Thr | Thr | Trp | Arg | Met | Met | Gln | Cys | Cys | Cys | Cys | Cys | Cys |
| | 2225 | 5 | | | | 2230 |) | | | | 2235 | <u> </u> | | | | 224 |
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| | Glu | Glu | Met | Pro | Pro | Pro | Pro | Pro | Pro | Ala | Leu | Leu | Ala | Ser | Thr | Thr |
| | | | | 2260 | | | | | 2265 | | | | | 2270 | | |
| | Lvs | His | Asn | Asn | Pro | Pro | Pro | Ser | Arq | Ser | Ser | His | Cys | Leu | Leu | Leu |
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